REMARKS

The Amendments

The claims are amended to more specify them to the examples provided in the specification and in the previously submitted declaration under 37 C.F.R. §1.132. It is noted that the further specificity renders the proviso at the end of claim 1 unnecessary and it is removed, greatly simplifying the claim. Support for the amendments is evident in the original disclosure and original claims since the groups are defined by variables specifically mentioned as optional for these groups.

Applicants reserve the right to file one or more continuing and/or divisional applications directed to any subject matter disclosed in the application which has been canceled by any of the above amendments.

The Restriction Requirement

Applicants note that the Office action fails to address applicants' previous further comments regarding the Restriction requirement. Applicants maintain their traversal of the restriction requirement and those previous arguments, which are incorporated herein by reference. Further, the greater specificity of the claims is believed to render the Election of Species/Restriction moot.

The Rejection under 35 U.S.C. §112, first paragraph

The rejection of claims 1-19 and 25-27 under 35 U.S.C. §112, first paragraph, for lack of

enablement, is respectfully traversed.

The claims have been greatly specified and simplified in their scope. The claims have not been limited to the very narrow scope indicated in the Office action to be enabled. But the amendments do limit the claims in a way to reflect that scope to some extent. The R^1, R^3, Y, n and m groups have been greatly specified and the claims otherwise specified to remove the need for the proviso. Applicants urge that the original disclosure, taken in light of the knowledge of one of ordinary skill in the art, and the previously submitted Declaration under 37 C.F.R. §1.132 support that the compounds, as currently claimed, would be reasonably expected to be useful for the intended use described in the specification, e.g., to treat HCV infection.

The evidence in the original disclosure and in the Declaration under 37 C.F.R. §1.132 previously submitted provide a representative showing from which one of ordinary skill in the art would have a reasonable expectation that the compounds, as currently claimed, would be useful in methods for treating hepatitis C viral infection in a mammal. The declaration and Examples 7 - 9 of the specification (see pages115-116) provide disclosures and data of the activity of a representative group of the compounds as claimed in several assays indicative of activity for treating hepatitis C viral infection. The specific data in the declaration shows activity on the cell-based luciferase reporter HCV RNA replication assay for compounds according to the claimed invention. A representative group of compounds were selected which show a variety of variables on the R^2, R^4, R^5 and R^6 substituents of applicants' general formula (I) – as noted above the R^1, R^3, Y, n and m groups have been greatly specified in the claims. Contrary to the unsupported allegation in the "Response to Applicants' Remarks" section of the Office action, this data shows that the compounds have similar activity even when the R^2 group is varied from phenyl to

bicyclic heteroaryl groups. Also, variable cyclic and non-cyclic groups for the R^4/R^6 combination are shown to exhibit activity in the assay. In reply to this evidence, the PTO has presented absolutely no evidence to suggest that the compounds would not exhibit the properties as disclosed by the inventors and presented absolutely no basis to refute the evidence presented by applicants.

Additionally, applicants reiterate that, even absent the above-discussed evidence, the PTO has still failed to meet its initial burden of proof to assert lack of enablement. The PTO has failed to provide any evidence or objective reasoning substantiating the allegation that the enabling disclosure is not commensurate in scope with the claims. See, e.g., MPEP §2164.04 citing In re Marzocchi et al., 169 USPQ 367 (CCPA 1971), establishing that applicants' disclosure of how to make and use the invention "*must* be taken as in compliance with the enabling requirement of the first paragraph of §112 *unless* there is reason to doubt the objective truth of the statements contained therein." The Office action does not set forth any reason to doubt the statements of the inventors in the specification regarding use of the invention. Further, the Office action fails to explain "*why* it doubts the truth or accuracy" of the inventors' statements of use in the specification. The "Response to Applicants' Remarks" section of the Office action alleges that the Examiner has provided evidence or objective reasoning to substantiate the allegation of lack of enablement because "the examiner stated above that alternative members of the genus of compounds of formula I for example, wherein R2 equals phenyl or naphthyl or furyl or thienyl are not obvious over one another and are therefore not expected to exhibit similar chemical properties." However, the Examiner's mere statement does not substitute for any evidence or objective proof of the assertion. This is especially the case

where the applicants have provided the above-discussed evidence which supports enablement while the PTO has provided no actual evidence at all to support its position. Absent any supportable reason or explanation for doubting the truth or accuracy of the inventors' disclosure, the PTO's initial burden is not met. In this case, the shifting of the burden of proof to applicants – as being alleged in the action – is improper. For at least these reasons, the rejection should be withdrawn.

Regarding the discussion of the factors a) – i) in the Office action, applicants have the following comments. However, regardless of these factors, the PTO has still not met the initial burden of proof to support the rejection for all of the above-discussed reasons.

The Office action states that determining if a particular compound within the claimed scope would be active would require making the compound and subjecting it to the NS3-NS4A protease assay. Further, the Office action states that such would require a "large amount" of experimentation. But applicants have disclosed the necessary assays to make this determination and it is merely a routine matter to perform the assays and evaluate any specific compound. The requirement of some experimentation, even a large amount, does not equate to **undue** experimentation or lack of enablement. Where the experimentation required is merely routine experimentation to one of ordinary skill in the art, it is not undue experimentation and does not support a case for lack of enablement. See, e.g., In re Wands, 858 F.2d at 736-37, 8 USPQ2d at 1404, stating: "Enablement is not precluded by the necessity for some experimentation ... . However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation'." See also Ex parte Jackson, 217 USPQ 804 (Bd. Pat. App. 1982), stating: "The determination of what constitutes undue experimentation in a

given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. ... The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed." As the Office action implicitly acknowledges, the specification here provides the guidance necessary to one of ordinary skill in the art to proceed with the required experimentation, i.e., the specification identifies the assays necessary to determine the activity of the compounds; see, e.g., page 115, line 20, to page 116, line 23. The specification also provides an adequate amount of direction on the manner of administration of the compounds (see, e.g., page 62, line 12, to page 66, line 8) and a large amount of detail and examples on how to make the compounds (see, e.g., page 66, line 10, to page 115, line 18).

The Office action states that the specification merely indicates an intent to make and use compounds limited by the variables recited at the top of page 6 of the Office action. However, a review of Tables 1-6 (pages 117-137) of the specification and the 37 C.F.R. §1.132 Declaration, as discussed above, makes clear that applicants made compounds which a much larger variety of variables. Also, the specification states (page 116, lines 10-14) that many of the compounds shown in those tables "were found to have IC50 values below 1 μM in the NS3-NS4A protease assay of Example 7." Representative compounds were also tested in the cell-based luciferase reporter HCV RNA replication assay of Example 8. Further, the Declaration under 37 C.F.R. §1.132 provides additional proof of the activity of compounds representative of the currently claimed scope. Thus, the compounds were tested to show their activity. Additionally, there is no

basis on the record to suggest the compounds, as claimed would not have this activity.

The Office action further indicates that lack of enablement is evidenced because the use of applicants' compounds is based on their physiological effect and that such use is inherently unpredictable. Applicants respectfully disagree that any use related to physiological activity is necessarily unpredictable to the extent of supporting lack of enablement. There is no evidence on the record to support such a statement. The Office action alleges that there is no reasonable basis to assume the scope of claimed compounds would share the same class of biological properties. However, as discussed above, applicants have provided the inventors' disclosure stating such use and a representative amount of evidence to support the disclosure. In view thereof, the PTO has provided no evidence to refute the inventors' statements or the representative assay data. The burden of proof lies with the PTO to make a case for non-enablement. The Office action alleges that the compounds are chemically non-equivalent but there is also no basis for this statement. Clearly, the compounds do share a large degree of structural similarity as shown by the general structural formula (I) of claim 1. Further, a representative amount of these compounds – with varying substitutents – have been shown to exhibit a shared biological activity in the assays. There is no evidence on the record to refute that such activity derives from the shared structural aspects of the compounds shown by applicants' formula (I). The standard for enablement is not absolute predictability but only reasonable expectation of success; see In re Wright, 999 F.2d 1557, 27 USPQ2d 1510,1512 (Fed.Cir. 1993). Applicants urge based on the above discussion that a reasonable expectation of success is supported on the record as a whole and that no evidence is provided by the PTO to indicate otherwise.

Finally, it would appear that the primary basis for alleging lack of enablement is that the

claims are allegedly of very broad scope. Applicants believe the claims, certainly as currently, amended, are not of an undue breadth. In any event, breadth alone is not a sufficient basis to support a lack of enablement rejection.

For all of the above reasons, applicants urge that applicants' disclosure provides one of ordinary skill in the art – considering the knowledge available in the art at the time of the invention – adequate teachings to make and use the claimed invention using only routine experimentation which is described in the disclosure. Thus, the instant claims are enabled and the rejection under 35 U.S.C. §112, first paragraph, should be withdrawn.

The Rejection under 35 U.S.C. §103

The rejection of claims 1-19 and 25-27 under 35 U.S.C. §103, as being obvious over Scola (U.S. Patent No. 7,132,504), is respectfully traversed.

From the "Response to Applicants Remarks" part of the Office action, applicants believe that their previous arguments have been misinterpreted. Further, the higher specificity of the claims due to the above amendments lends further strength to applicants' argument for a distinctive selection invention within Scola.

Applicants do not dispute that Scola generically encompasses the possibility that its B group can be –C(=O)-O-cycloalkyl, among many other possibilities. Applicants point is that Scola does not actually fairly suggest compounds where the B group is –C(=O)-O-cycloalkyl since its scope is so broad and there is no direction to any compounds other than those where B is –C(=O)-O-unsubstituted alkyl. Such compounds are expressly excluded from the scope of the instant claims by the proviso on the definition of B in claim 1.

Scola provides a broad generic formula (I) defined at cols. 2-3. However, the only compounds specifically exemplified or otherwise specifically defined by Scola are those where the B group of Scola is –C(=O)-O-alkyl with alkyl being methyl or tert-butyl. See the disclosure at col. 12, lines 2-3, and the Examples at cols. 57-72. Of the 26 compounds Scola discloses having a specific B group, in everyone of them B is –C(=O)-O-alkyl with alkyl being methyl or tert-butyl.

Applicants urge that – despite its broad generic formula – Scola does not provide a disclosure which fairly suggests the claimed invention and, thus, does not render the claimed invention obvious under 35 U.S.C. §103. As was clearly set forth in In re Jones, 21 USPQ 2d 1941 (Fed. Cir. 1992), it is not the law that ".. regardless of how broad, a disclosure of a chemical genus renders obvious any species which happens to fall within it." Instead, the disclosure must be considered as a whole as to whether it fairly suggests the claimed invention to one of ordinary skill in the art; see also In re Baird, 29 USPQ2d 1550 (Fed. Cir. 1994). As in Jones and Baird, the reference provided a generic disclosure which encompassed a very large number of compounds, there were no specific teachings in the reference to suggest the specific selection of variables necessary to arrive at the claimed compounds. In view of the further specificity of the claims by the above amendments, the failure of the reference to direct one of ordinary skill in the art to the selection of the variables which will result in the claimed invention is even more evident. In fact, the reference indicates a preference for compounds which are particularly excluded from the claimed compounds. In view of the preferences and examples disclosed in Scola, applicants urge that the facts are analogous to Jones and Baird. Therefore, as the Courts concluded in Jones and Baird, the reference does not fairly suggest the claimed compounds and,

thus, does not render the claimed invention prima facie obvious. Accordingly, the rejection under 35 U.S.C. §103 over Scola should also be withdrawn.

Regarding claim 11, additional basis for nonobviousness is provided. Scola fails to give any suggestion of compounds having the type of heterocyclic group described for the R^2 substituent in this claim. Applicants made this argument previously but the Office action fails to address at all these separate arguments for claim 11. Such consideration is urged.

The Rejections for Obviousness-type Double Patenting and under 35 U.S.C. §102(e)

The rejection of claims 1-19 and 25 over U.S. Ser. No. 11/766,171, provisionally for obviousness-type double patenting, and the rejection of claims 1-13 and 15-19 over Llinas-Brunet (US Pub. No. 2007/0243166) for anticipation under 35 U.S.C. §102(e), are respectfully traversed. The US Pub. No. 2007/0243166 is the publication of the 11/766,171 application and both are referred to below as "Llinas-Brunet."

Applicants respectfully note that, contrary to the statement in the Office action, the compounds defined by the instant claims do not overlap in scope with the compounds claimed or disclosed in the Llinas-Brunet application. Specifically, the compounds of the copending application require a substituted thiazole group on the quinoline ring; see formula I and the R2 group substituted on the thiazole ring in the claims and disclosure of the copending application. Such claims were previously excluded from the instant claims by the proviso in claim 1. With the above amendments to claim 1, however, such compounds are excluded from the claim scope without the need of the proviso. The R200 group no longer include Het as one of the possible substituents. Thus, the R20 group cannot be Het substituted by another Het which would be

required to achieve the quinoline substituted by thiazole structure of the copending application compounds.

Absent any overlap in the claims' scope, there is clearly no anticipation and no support for the rejection under 35 U.S.C. §102(e). Further, applicants urge that there is no support for the obviousness-type double patenting or obviousness rejection. The instant claims do not cover the compounds substituted as described in the Llinas-Brunet application. Furthermore, there is no suggestion from the Llinas-Brunet application to modify the Llinas-Brunet application compounds to arrive at the compounds of the instant claims. Thus, the provisional obviousness-type double patenting rejection and the rejection under 35 U.S.C. §102(e) should be withdrawn.

It is submitted that the claims are in condition for allowance. However, the Examiner is kindly invited to contact the undersigned to discuss any unresolved matters.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,

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